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> d his


     (FILE 'HOME' ENTERED AT 11:34:39 ON 22 SEP 1997)

     FILE 'WPIDS' ENTERED AT 11:35:22 ON 22 SEP 1997
L1             1 S WO9318210/PN
               E GILL P/IN
L2           324 S TAXOL
L3             0 S E3 AND L2
L4             7 S E3
               E GILL P S/IN
L5             1 S E3
L6            90 S METHOD AND L2
L7             0 S NEUTROPENIA AND L6
L8           742 S KAPOSIS (W) SARCOMA OR KS
L9             0 S L8 AND L2
L10           43 S PACLITAXEL
L11           15 S L10 AND L2
```

> d l5 1-28 ti

US PAT NO: 5,667,809 :IMAGE AVAILABLE: L5: 1 of 28
TITLE: Continuous fluorochemical microdispersions for the delivery of lipophilic pharmaceutical agents

US PAT NO: 5,658,947 :IMAGE AVAILABLE: L5: 2 of 28
TITLE: **Method** and composition for selectively inhibiting melanoma using betalinic acid

US PAT NO: 5,656,651 :IMAGE AVAILABLE: L5: 3 of 28
TITLE: Androgenic directed compositions

US PAT NO: 5,653,998 :IMAGE AVAILABLE: L5: 4 of 28
TITLE: Injectable liposomal pharmaceutical preparations

US PAT NO: 5,652,248 :IMAGE AVAILABLE: L5: 5 of 28
TITLE: **Method** of preventing peripheral neuropathies induced by anticancer agents

US PAT NO: 5,651,986 :IMAGE AVAILABLE: L5: 6 of 28
TITLE: Controlled local delivery of chemotherapeutic agents for treating solid tumors

US PAT NO: 5,646,176 :IMAGE AVAILABLE: L5: 7 of 28
TITLE: Phosphonooxymethyl ethers of taxane derivatives

US PAT NO: 5,635,531 :IMAGE AVAILABLE: L5: 8 of 28
TITLE: 3'-aminocarbonyloxy paclitaxels

US PAT NO: 5,626,862 :IMAGE AVAILABLE: L5: 9 of 28
TITLE: Controlled local delivery of chemotherapeutic agents for treating solid tumors

US PAT NO: 5,622,986 :IMAGE AVAILABLE: L5: 10 of 28
TITLE: 2'-and/or 7-substituted taxanes

US PAT NO: 5,620,875 :IMAGE AVAILABLE: L5: 11 of 28
TITLE: Transfer of **taxol** from yew tree cuttings into a culture medium over time

US PAT NO: 5,616,330 :IMAGE AVAILABLE: L5: 12 of 28
TITLE: Stable oil-in-water emulsions incorporating a taxine (**taxol**) and **method** of making same

US PAT NO: 5,602,272 :IMAGE AVAILABLE: L5: 13 of 28
TITLE: Reduction and resolution methods for the preparation of compounds useful as intemediates for preparing taxanes

US PAT NO: 5,580,899 :IMAGE AVAILABLE: L5: 14 of 28
TITLE: Hydrophobic taxane derivatives

US PAT NO: 5,569,720 :IMAGE AVAILABLE: L5: 15 of 28
TITLE: Polymer-bound **paclitaxel** derivatives

US PAT NO: 5,565,478 :IMAGE AVAILABLE: L5: 16 of 28
TITLE: Combination therapy using signal transduction inhibitors with **paclitaxel** and other taxane analogs

US PAT NO: 5,561,055 :IMAGE AVAILABLE: L5: 17 of 28
TITLE: Bacterial mass production of taxanes with Erwinia

US PAT NO: 5,547,981 :IMAGE AVAILABLE: L5: 18 of 28
TITLE: **Taxol**-7-carbazates

US PAT NO: 5,543,152 :IMAGE AVAILABLE: L5: 19 of 28
TITLE: Sphingosomes for enhanced drug delivery

US PAT NO: 5,534,499 :IMAGE AVAILABLE: L5: 20 of 28
TITLE: Lipophilic drug derivatives for use in liposomes

US PAT NO: 5,504,102 :IMAGE AVAILABLE: L5: 21 of 28
TITLE: Stabilized pharmaceutical composition and stabilizing solvent

US PAT NO: 5,489,589 :IMAGE AVAILABLE: L5: 22 of 28
TITLE: Amino acid derivatives of **paclitaxel**

US PAT NO: 5,473,055 :IMAGE AVAILABLE: L5: 23 of 28
TITLE: Polymer-bound **paclitaxel** derivatives

US PAT NO: 5,468,769 :IMAGE AVAILABLE: L5: 24 of 28
TITLE: **Paclitaxel** derivatives

US PAT NO: 5,395,850 :IMAGE AVAILABLE: L5: 25 of 28
TITLE: 6,7-epoxy paclitaxels

US PAT NO: 5,380,751 :IMAGE AVAILABLE: L5: 26 of 28
TITLE: 6,7-modified paclitaxels

US PAT NO: 5,362,831 :IMAGE AVAILABLE: L5: 27 of 28
TITLE: Polymer-bound **paclitaxel** derivatives

US PAT NO: 5,324,739 :IMAGE AVAILABLE: L5: 28 of 28
TITLE: Compound exhibiting antiproliferative activity against

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=> d his

     (FILE 'USPAT' ENTERED AT 13:54:50 ON 22 SEP 1997)
L1           394 S TAXOL
L2            33 S PACLITAXEL
L3            30 S L1 AND L2
L4       1064974 S METHOD
L5            28 S L4 AND L3
L6           263 S NEUTROPENIA
L7            28 S L5 AND L5
L8             3 S L6 AND L5
L9          3609 S KAPOSIS SARCOMA OR KS
L10            1 S L7 AND L9
L11            1 S L9 AND L5
```

=> d l8 1-3 ab

US PAT NO: 5,651,986 :IMAGE AVAILABLE: L8: 1 of 3

ABSTRACT:
A **method** and devices for localized delivery of a chemotherapeutic agent to solid tumors, wherein the agent does not cross the blood-brain barrier and is characterized by poor bioavailability and/or short half-lives in vivo, are described. The devices consist of reservoirs which release drug over an extended time period while at the same time preserving the bioactivity and bioavailability of the agent. In the most preferred embodiment, the device consists of biodegradable polymeric matrixes, although reservoirs can also be formulated from non-biodegradable polymers or reservoirs connected to implanted infusion pumps. The devices are implanted within or immediately adjacent the tumors to be treated or the site where they have been surgically removed. The examples demonstrate the efficacy of **paclitaxel** and camptothecin delivered in polymeric implants prepared by compression molding of biodegradable and non-biodegradable polymers, respectively. The results are highly statistically significant.

US PAT NO: 5,626,862 :IMAGE AVAILABLE: L8: 2 of 3

ABSTRACT:
A **method** and devices for localized delivery of a chemotherapeutic agent to solid tumors, wherein the agent does not cross the blood-brain barrier and is characterized by poor bioavailability and/or short half-lives in vivo, are described. The devices consist of reservoirs which release drug over an extended time period while at the same time preserving the bioactivity and bioavailability of the agent. In the most preferred embodiment, the device consists of biodegradable polymeric matrixes, although reservoirs can also be formulated from non-biodegradable polymers or reservoirs connected to implanted infusion pumps. The devices are implanted within or immediately adjacent the tumors to be treated or the site where they have been surgically removed. The examples demonstrate the efficacy of **paclitaxel** and camptothecin delivered in polymeric implants prepared by compression molding of biodegradable and non-biodegradable polymers, respectively. The results are highly statistically significant.

US PAT NO: 5,565,478 :IMAGE AVAILABLE: L8: 3 of 3

ABSTRACT:
The present invention provides compositions and methods for the treatment of cancer in a subject wherein compounds of formula I defined herein in combination with **paclitaxel** or other modified taxane analogs provide enhanced anticancer effects over the effects achieved with the individual compounds.

d l1 1-11 all

L1 ANSWER 1 OF 11 MEDLINE
AN 97340903 MEDLINE
TI Effects of human immunodeficiency virus and colony-stimulating factors on the production of interleukin 6 and tumor necrosis factor alpha by monocyte/macrophages.
AU Foli A; **Saville M W**; May L T; Webb D S; Yarchoan R
CS HIV and AIDS Malignancy Branch, National Cancer Institute, Bethesda, Maryland 20892, USA.
NC AI16262 (NIAID)
SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1997 Jul 1) 13 (10) 829-39. Journal code: ART. ISSN: 0889-2229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9710
EW 19971005
AB Patients infected with human immunodeficiency virus (HIV) frequently have increased production of interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-alpha), and these cytokines may in turn contribute to the disease pathogenesis. It has been hypothesized that secretion of these cytokines by HIV-exposed mononuclear cells or HIV-infected monocyte/macrophages (M/Ms) is the principal source of their overproduction in HIV-infected patients, and the present study was undertaken to explore this issue. We observed that in the absence of endotoxin or cytokines, M/Ms productively infected by HIV do not produce detectable IL-6 or TNF-alpha. However, granulocyte-macrophage colony-stimulating factor (GM-CSF), a cytokine that enhances HIV replication in M/Ms and is frequently used to propagate monocytotropic strains of HIV, can induce the relatively long-term production of IL-6 (up to 47 U/ml) and TNF-alpha (up to 47 pg/ml) by M/Ms, even in the absence of HIV. Also, HIV induced production of a relatively small (< or = 9 U/ml) quantity of IL-6 in M/Ms stimulated with macrophage-colony stimulating factor (M-CSF). Finally, while highly concentrated HIV induced production of both cytokines by either M/Ms or peripheral blood mononuclear cells (PBMCs), this production was almost completely eliminated when care was taken to avoid contamination of HIV by endotoxin. These data suggest that the excess IL-6 and TNF-alpha in HIV-infected patients does not simply result from their production by HIV-infected M/Ms and that alternative mechanisms are involved in this process.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cells, Cultured
*Colony-Stimulating Factors: PD, pharmacology
Cytokines: BI, biosynthesis
Endotoxins: IP, isolation & purification
Endotoxins: TO, toxicity
Granulocyte-Macrophage Colony-Stimulating Factor: PD, pharmacology
HIV Infections: ET, etiology
HIV Infections: IM, immunology
HIV-1: IP, isolation & purification
*HIV-1: PY, pathogenicity
*Interleukin-6: BI, biosynthesis
Macrophage Colony-Stimulating Factor: PD, pharmacology
Macrophages: DE, drug effects

> s taxol
L1 403 TAXOL

=> s method and l1
1067788 METHOD
L2 378 METHOD AND L1

=> d l2 1-10

1. 5,672,584, Sep. 30, 1997, Cyclic prodrugs of peptides and peptide nucleic acids having improved metabolic stability and cell membrane permeability; Ronald T. Borchardt, et al., 514/11; 530/317 [IMAGE AVAILABLE]

2. 5,670,673, Sep. 23, 1997, **Method** for the isolation and purification of **taxol** and its natural analogues; Koppaka V. Rao, 549/510; 210/656, 660; 560/107 [IMAGE AVAILABLE]

3. 5,670,663, Sep. 23, 1997, Recovery of taxanes from conifers; Don J. Durzan, et al., 549/332, 510; 560/248 [IMAGE AVAILABLE]

4. 5,670,653, Sep. 23, 1997, Process for the manufacture of (4,5)-trans-oxazolidines; Hans Hilpert, 548/229, 230 [IMAGE AVAILABLE]

5. 5,670,537, Sep. 23, 1997, **Method** for effecting tumor regression with a low dose, short infusion **taxol** regimen; Renzo Mauro Canetta, et al., 514/149 [IMAGE AVAILABLE]

6. 5,670,536, Sep. 23, 1997, Pharmaceutical composition based on taxoids; Manfred Durr, et al., 514/449; 549/510 [IMAGE AVAILABLE]

7. 5,670,507, Sep. 23, 1997, **Method** for reversing multiple drug resistant phenotype; Glenn C. Rice, et al., 514/263, 274, 299, 310, 315, 418 [IMAGE AVAILABLE]

8. 5,670,502, Sep. 23, 1997, **Method** of tumor treatment; J. Martin Brown, 514/243, 81, 234.2, 235.2, 492 [IMAGE AVAILABLE]

9. 5,670,349, Sep. 23, 1997, HMG2 promoter expression system and post-harvest production of gene products in plants and plant cell cultures; Carole Lyn Cramer, et al., 435/172.3, 69.1, 320.1; 536/23.1, 24.1; 800/205 [IMAGE AVAILABLE]

10. 5,667,809, Sep. 16, 1997, Continuous fluorochemical microdispersions for the delivery of lipophilic pharmaceutical agents; Leo A. Trevino, et al., 424/501, 423, 427, 430, 435, 436, 443, 451, 464; 514/937 [IMAGE

Macrophages: IM, immunology
Monocytes: DE, drug effects
Monocytes: IM, immunology
*Tumor Necrosis Factor: BI, biosynthesis
RN 81627-83-0 (Macrophage Colony-Stimulating Factor); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
CN 0 (Colony-Stimulating Factors); 0 (Cytokines); 0 (Endotoxins); 0 (Interleukin-6); 0 (Tumor Necrosis Factor)

L1 ANSWER 2 OF 11 MEDLINE
AN 97170239 MEDLINE
TI The pharmacokinetics of TNP-470, a new angiogenesis inhibitor.
AU Figg W D; Pluda J M; Lush R M; **Saville M W**; Wyvill K; Reed E; Yarchoan R
CS Clinical Pharmacokinetics Section, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
SO PHARMACOTHERAPY, (1997 Jan-Feb) 17 (1) 91-7.
Journal code: PAR. ISSN: 0277-0008.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9706
EW 19970602
AB STUDY OBJECTIVE: To characterize the pharmacokinetic profile of TNP-470, a synthetic analog of fumagillin that is a potent inhibitor of angiogenesis and inhibits neovascularization in several solid tumor models. DESIGN: A dose-escalation phase I clinical trial. SETTING: The National Institutes of Health. PATIENTS: Patients with human immunodeficiency virus-associated Kaposi's sarcoma. INTERVENTIONS: The TNP-470 dosage was increased in 13 sequential cohorts using a modified Fibonacci escalation scheme (4.6, 9.3, 15.4, 23.2, and 43.1 mg/m2). The drug was administered as a 1-hour intravenous infusion. Serial blood samples were collected and assayed by reverse-phase high-performance liquid chromatography and the pharmacokinetics were characterized. MEASUREMENTS AND MAIN RESULTS: There was a linear relationship between the dose of TNP-470 and both area under the curve to infinity (AUC[inf]) and time to maximum concentration (Cmax). The Cmax ranged between 6.6 ng/ml at the lowest dosage (4.6 mg/m2) and 597.1 ng/ml at the highest dosage (43.1 mg/m2). The agent was rapidly cleared from the circulation with a short terminal half-life (0.88 +/- 2.5 hr), which is consistent with preclinical data. Peak plasma concentrations of AGM-1883, an active metabolite, ranged between 0.4 and 158.1 ng/ml. CONCLUSION: Concentrations of TNP-470 that have in vitro activity were achievable in vivo. The drug was rapidly cleared from the circulation after a single 1-hour infusion. There was considerable interpatient variability in the clearance, but no evidence of saturable elimination. If more prolonged exposure is necessary for activity, administration of TNP-470 by continuous infusion may be suitable.
CT Check Tags: Human; Male; Support, U.S. Gov't, Non-P.H.S.
Adult
*Antibiotics, Antineoplastic: PK, pharmacokinetics
Antibiotics, Antineoplastic: TU, therapeutic use
*HIV Infections: CO, complications
Middle Age
*Neovascularization, Pathologic: PC, prevention & control
*Sarcoma, Kaposi's: BS, blood supply
Sarcoma, Kaposi's: DT, drug therapy
Sarcoma, Kaposi's: ET, etiology
*Sesquiterpenes: PK, pharmacokinetics
Sesquiterpenes: TU, therapeutic use

RN 129298-91-5 (AGM 1470)
CN 0 (Antibiotics, Antineoplastic); 0 (Sesquiterpenes)

L1 ANSWER 3 OF 11 MEDLINE
AN 97046247 MEDLINE
TI In vitro selection and molecular characterization of human immunodeficiency virus type 1 with reduced sensitivity to 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA).
AU Foli A; Sogocio K M; Anderson B; Kavlick M; **Saville M W**; Wainberg M A; Gu Z; Cherrington J M; Mitsuya H; Yarchoan R
CS Medicine Branch, National Cancer Institute, Bethesda, MD 20892-1906, USA.
SO ANTIVIRAL RESEARCH, (1996 Oct) 32 (2) 91-8.
Journal code: 6I7. ISSN: 0166-3542.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9704
EW 19970403
AB 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA) is an acyclic nucleotide with potent in vitro activity against human immunodeficiency virus type 1 (HIV-1). The present study was undertaken to determine whether HIV-1 resistance to PMEA could be generated by in vitro selection and if so, to determine which mutations in reverse transcriptase (RT) were responsible. HIV-1LAI was serially passaged for 10 months in the presence of increasing concentrations of PMEA up to a maximum of 40 microM. After 40 passages, the 50% inhibitory concentration (IC50) of PMEA had increased almost 7-fold from 4.45 to 30.5 microM. Some cross-resistance to 2',3'-dideoxycytidine (ddC, zalcitabine), 2',3-dideoxyinosine (ddI, didanosine), and 3'-thiacytidine (3TC, lamivudine) was also observed, but no cross-reactive resistance to 3'-azido-3'-thymidine (AZT, zidovudine). Sequencing of the RT encoding region of each of eight pol clones from resistant isolates revealed a Lys-65-->Arg (K65R) substitution. HIV with the K65R mutation inserted by site-directed mutagenesis also had decreased sensitivity to PMEA in H9 cells and a similar cross-resistance profile. Thus, HIV can develop decreased sensitivity to PMEA after long-term in vitro exposure and this change is associated with a K65R substitution. Additional studies will be needed to determine whether a similar mutation in HIV RT develops in patients receiving PMEA or its orally bioavailable prodrug adefovir dipivoxil (bis-POM PMEA).
CT Check Tags: Human; Support, Non-U.S. Gov't
*Adenine: AA, analogs & derivatives
Adenine: PD, pharmacology
Amino Acid Sequence
*Anti-HIV Agents: PD, pharmacology
Cell Line
Drug Resistance, Microbial: GE, genetics
*HIV-1: DE, drug effects
HIV-1: EN, enzymology
HIV-1: GE, genetics
HIV-1 Reverse Transcriptase: GE, genetics
HIV-1 Reverse Transcriptase: ME, metabolism
Molecular Sequence Data
Point Mutation
Serial Passage
RN 106941-25-7 (9-(2-phosphonylmethoxyethyl)adenine); 73-24-5 (Adenine)
CN EC 2.7.7.- (HIV-1 Reverse Transcriptase); 0 (Anti-HIV Agents)

L1 ANSWER 4 OF 11 MEDLINE
AN 96420595 MEDLINE
TI HIV infection--induced posttranslational modification of T cell signaling molecules associated with disease progression.

AU Stefanova I; **Saville M W**; Peters C; Cleghorn F R; Schwartz D; Venzon D J; Weinhold K J; Jack N; Bartholomew C; Blattner W A; Yarchoan R; Bolen J B; Horak I D

CS National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.. IStefanova@pop.niaid.nih.gov

SO JOURNAL OF CLINICAL INVESTIGATION, (1996 Sep 15) 98 (6) 1290-7. Journal code: HS7. ISSN: 0021-9738.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals

EM 9701

EW 19970104

AB In attempt to elucidate the mechanism of the HIV infection induced T cell unresponsiveness, we studied signal-transducing molecules proximal to the T cell receptor (TCR) in T lymphocytes of HIV-infected individuals. Total amounts of protein tyrosine kinases (PTKs) Lck, Fyn, and ZAP-70 and the zeta chain of the TCR were found significantly decreased in T cells of symptomatic/AIDS patients as well as in T cells of individuals in acute and early asymptomatic stages of HIV infection. Unexpectedly, the detection of Lck, Fyn, and ZAP-70 was reversed after the treatment of cell lysates with dithiothreitol. This suggests that PTKs Lck, Fyn, and ZAP-70 were modified by a mechanism altering the status of sulfhydryl groups. Moreover, this mechanism seems to affect selectively T cells of HIV infected patients since B cell PTKs Syk and Lyn were detected structurally and functionally intact. Interestingly, similar alterations of signaling molecules were not detected in T cells of HIV-infected long-term asymptomatic individuals. Modification of T cell PTKs may thus underlie the HIV-induced impairment of lymphocyte function and may potentially predict disease progression.

CT Check Tags: Human
src-Family Kinases: AN, analysis
src-Family Kinases: IM, immunology
B-Lymphocytes: IM, immunology
B-Lymphocytes: PH, physiology
Disease Progression
*HIV Infections: IM, immunology
*HIV-1
Immunoblotting
Phosphorylation
Polymerase Chain Reaction
*Protein Processing, Post-Translational: IM, immunology
Protein-Tyrosine Kinase: AN, analysis
Protein-Tyrosine Kinase: IM, immunology
Proto-Oncogene Proteins: AN, analysis
Proto-Oncogene Proteins: IM, immunology
Receptors, Antigen, T-Cell: IM, immunology
Receptors, Antigen, T-Cell: PH, physiology
Receptors, Antigen, T-Cell, gamma-delta: AN, analysis
Receptors, Antigen, T-Cell, gamma-delta: IM, immunology
*Signal Transduction: IM, immunology
Sulfhydryl Compounds: ME, metabolism
*T-Lymphocytes: IM, immunology
*T-Lymphocytes: PH, physiology

CN EC 2.7.1.- (lymphocyte specific protein tyrosine kinase p56(lck)); EC 2.7.1.- (src-Family Kinases); EC 2.7.1.- (ZAP-70 kinase); EC 2.7.1.112 (Protein-Tyrosine Kinase); 0 (proto-oncogene protein c-fyn); 0 (Proto-Oncogene Proteins); 0 (Receptors, Antigen, T-Cell); 0 (Receptors, Antigen, T-Cell, gamma-delta); 0 (Sulfhydryl Compounds)

L1 ANSWER 5 OF 11 MEDLINE

AN 96369161 MEDLINE

TI Immune-based therapies for treatment of HIV infection.

AU Piscitelli S C; Minor J R; **Saville M W**; Davey R T Jr
CS Department of Pharmacy, Warren G Magnuson Clinical Center, National Institutes of Health, Bethesda, MD 20892, USA.
SO ANNALS OF PHARMACOTHERAPY, (1996 Jan) 30 (1) 62-76. Ref: 45
Journal code: BBX. ISSN: 1060-0280.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 9612
AB OBJECTIVE: To review the in vitro, animal, and clinical data on immune-based therapies for treatment of HIV infection. DATA SOURCES: An extensive MEDLINE search was performed for interleukins, interferons, immunotoxins, tumor necrosis factor (TNF)-directed agents, vaccines, and gene therapy. STUDY SELECTION: In vitro experiments with immune-based agents in cell lines infected with HIV were included. In addition, all human studies and case reports that used these agents in patients infected with HIV were selected. Additional literature included abstracts from international meetings on HIV and AIDS. DATA EXTRACTION: Data regarding activity, efficacy, and toxicity were extracted from in vitro and in vivo studies. When conflicting data were observed, both viewpoints were stated to give an unbiased analysis. Because HIV research involves multiple social, ethical, and scientific issues, perspectives on these problems were addressed, where appropriate. DATA SYNTHESIS: Current antiretroviral therapy is limited to short-term responses and has minimal effect on overall survival. Because the human immune response to HIV infection is effective at keeping the virus suppressed for a number of years, a focus of HIV research has been to examine immune-based therapies for treatment of HIV infection that attempt to augment enhance, or boost the patient's immune system. Interleukins, interferons, immunotoxins, TNF-directed therapies, vaccines, and gene therapy have been studied in patients infected with HIV. Properties shared among these therapeutic modalities include adverse effect profiles, response rates dependent on baseline immunocompetence, the potential to activate viral replication, the need for supportive care, and sensitive laboratory tests required for monitoring. CONCLUSIONS: Immune-based agents represent a new approach to the treatment of HIV infection. Whereas antiretrovirals only inhibit viral replication, these agents are designed to enhance the immune system of the patient. Future attempts to manage HIV infection may combine standard nucleoside analogs with immune-based therapies.
CT Check Tags: Animal; Human
Adjuvants, Immunologic: TU, therapeutic use
AIDS Vaccines: TU, therapeutic use
Gene Therapy
*HIV Infections: TH, therapy
*Immunotherapy
Immunotoxins: TU, therapeutic use
CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (Immunotoxins)

L1 ANSWER 6 OF 11 MEDLINE
AN 96290436 MEDLINE
TI Kaposi's sarcoma (KS)-associated herpesvirus-like DNA sequences in peripheral blood mononuclear cells: association with KS and persistence in patients receiving anti-herpesvirus drugs.
AU Humphrey R W; O'Brien T R; Newcomb F M; Nishihara H; Wyvill K M; Ramos G A; **Saville M W**; Goedert J J; Straus S E; Yarchoan R
CS Medicine Branch National Cancer Institute, National Institutes of Health, Bethesda, MD 20892-1906, USA.
SO BLOOD, (1996 Jul 1) 88 (1) 297-301.
Journal code: A8G. ISSN: 0006-4971.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9611
AB Herpesvirus-like DNA sequences (KSHV/HHV-8) have recently been described in AIDS-associated Kaposi's sarcoma (KS) lesions. Many questions remain regarding the role of this virus in KS and the therapeutic implications of this finding. In the current study, KSHV/HHV-8 DNA was detected in peripheral blood mononuclear cells (PBMCs) from human immunodeficiency virus (HIV)-infected patients with KS (34/98) more often than in HIV-infected individuals without KS (12/64, P = .03). The detection of KSHV/HHV-8 DNA did not correlate with the CD4 lymphocyte count. Five patients demonstrated KSHV/HHV-8 DNA in their PBMCs during administration of intravenous foscarnet and/or ganciclovir. The continued detection of KSHV/HHV-8 DNA in the PBMCs of patients receiving these anti-herpesvirus drugs has potential implications regarding the virus-cell relationship of KSHV/HHV-8, as well as for the value of these drugs in treating or preventing KS, but additional studies are needed.
CT Check Tags: Comparative Study; Female; Human; Male
*Acquired Immunodeficiency Syndrome: CO, complications
Adult
Antiviral Agents: PD, pharmacology
*Antiviral Agents: TU, therapeutic use
Base Sequence
Blood Coagulation Disorders: BL, blood
Blood Coagulation Disorders: CO, complications
Cohort Studies
*DNA, Viral: IP, isolation & purification
Foscarnet: PD, pharmacology
Foscarnet: TU, therapeutic use
Ganciclovir: PD, pharmacology
Ganciclovir: TU, therapeutic use
Herpesviridae: DE, drug effects
*Herpesviridae: IP, isolation & purification
Herpesviridae Infections: BL, blood
Herpesviridae Infections: DT, drug therapy
Herpesviridae Infections: EP, epidemiology
*Herpesviridae Infections: VI, virology
Homosexuality
HIV Seronegativity
*Leukocytes, Mononuclear: VI, virology
Molecular Sequence Data
Prevalence
Risk Factors
Sarcoma, Kaposi's: ET, etiology
Sarcoma, Kaposi's: PA, pathology
*Sarcoma, Kaposi's: VI, virology
Skin Neoplasms: ET, etiology
Skin Neoplasms: PA, pathology
*Skin Neoplasms: VI, virology
RN 4428-95-9 (Foscarnet); 82410-32-0 (Ganciclovir)
CN 0 (Antiviral Agents); 0 (DNA, Viral)

L1 ANSWER 7 OF 11 MEDLINE
AN 95363479 MEDLINE
TI Phase I/II study of intermittent all-trans-retinoic acid, alone and in combination with interferon alfa-2a, in patients with epidemic Kaposi's sarcoma.
AU Bailey J; Pluda J M; Foli A; **Saville M W**; Bauza S; Adamson P C; Murphy R F; Cohen R B; Broder S; Yarchoan R
CS Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SO JOURNAL OF CLINICAL ONCOLOGY, (1995 Aug) 13 (8) 1966-74.

Journal code: JCO. ISSN: 0732-183X.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9511
AB PURPOSE: A phase I/II study of oral all-trans-retinoic acid (ATRA; tretinoin), administered every other week alone and then in combination with interferon (IFN) alfa-2a, was undertaken to evaluate the activity, toxicity, and pharmacokinetics of this regimen in patients with human immunodeficiency virus (HIV)-associated Kaposi's sarcoma (KS). PATIENTS AND METHODS: Thirteen patients with HIV-associated KS, eight of whom had more than 100 CD4 cells/microL, were entered. The protocol initially called for patients to receive 150 mg/m2/d of ATRA every other week. However, this regimen was associated with headaches, and the initial dose of ATRA was reduced to 40 mg/m2/d orally in three divided doses, increasing to a maximum of 100 mg/m2/d. After 12 weeks, IFN alfa-2a could be added. RESULTS: The principal toxicities from ATRA were headaches (12 patients) and dry skin or lip (seven patients). Of 12 assessable patients, 10 had progressive disease and two had stable disease on ATRA alone. One of eight assessable patients who went on to receive ATRA plus IFN alfa-2a had partial response (PR). There were no overall changes in the serum HIV p24 antigen (Ag) level or CD4 count during treatment with ATRA alone. Peak ATRA levels decreased during the week of continuous ATRA therapy, but rebounded when treatment was resumed after a week without the drug. CONCLUSION: Intermittent ATRA therapy was reasonably well tolerated and provided a means to circumvent the low plasma exposure found with continuous ATRA therapy. However, we were unable to document antitumor activity in patients with HIV-associated KS.
CT Check Tags: Human; Male
Adult
Combined Modality Therapy
Drug Administration Schedule
Headache: CI, chemically induced
HIV: DE, drug effects
HIV: PH, physiology
HIV Infections: CO, complications
*Interferon Alfa-2a: TU, therapeutic use
Least-Squares Analysis
Middle Age
Regression Analysis
Remission Induction
*Sarcoma, Kaposi's: DT, drug therapy
Sarcoma, Kaposi's: ET, etiology
Sarcoma, Kaposi's: TH, therapy
Sarcoma, Kaposi's: VI, virology
*Tretinoin: AD, administration & dosage
Tretinoin: AE, adverse effects
Tretinoin: PK, pharmacokinetics
Virus Replication: DE, drug effects
RN 302-79-4 (Tretinoin); 76543-88-9 (Interferon Alfa-2a)

L1 ANSWER 8 OF 11 MEDLINE
AN 95326733 MEDLINE
TI Treatment of HIV-associated Kaposi's sarcoma with paclitaxel.
AU **Saville M W**; Lietzau J; Pluda J M; Feuerstein I; Odom J; Wilson W H; Humphrey R W; Feigal E; Steinberg S M; Broder S; et al
CS National Cancer Institute, Bethesda, MD 20892, USA.
SO LANCET, (1995 Jul 1) 346 (8966) 26-8.
Journal code: L0S. ISSN: 0140-6736.

CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9510
AB We investigated whether paclitaxel was active in AIDS-associated Kaposi's sarcoma. We gave 135 mg/m2 intravenously over 3 hours every 21 days. Follow-up is available on the first 20 patients, most of whom had advanced Kaposi's sarcoma and severe immunocompromise. Neutropenia was the most frequent dose-limiting toxic effect; novel toxic effects included late fevers, rash, and eosinophilia. Creatinine increased in 2 patients and 1 patient had cardiomyopathy. There were 13 partial responses (65%, 95% CI 41-85%). All 5 patients with pulmonary involvement responded. Paclitaxel appears to be active against Kaposi's sarcoma as a single agent. Further studies, including a randomised trial, are warranted.
CT Check Tags: Human; Male; Support, Non-U.S. Gov't
Acquired Immunodeficiency Syndrome: CO, complications
Adult
Cimetidine: AD, administration & dosage
Dexamethasone: AD, administration & dosage
Diphenhydramine: AD, administration & dosage
Drug Therapy, Combination
*HIV Infections: CO, complications
*HIV-1
*Lung Neoplasms: DT, drug therapy
Middle Age
*Paclitaxel: AD, administration & dosage
Paclitaxel: AE, adverse effects
*Sarcoma, Kaposi's: DT, drug therapy
RN 33069-62-4 (Paclitaxel); 50-02-2 (Dexamethasone); 51481-61-9 (Cimetidine); 58-73-1 (Diphenhydramine)

L1 ANSWER 9 OF 11 MEDLINE
AN 95235035 MEDLINE
TI Effects of the Th1 and Th2 stimulatory cytokines interleukin-12 and interleukin-4 on human immunodeficiency virus replication.
AU Foli A; **Saville M W**; Baseler M W; Yarchoan R
CS Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SO BLOOD, (1995 Apr 15) 85 (8) 2114-23.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9507
AB The cytokines interleukin-12 (IL-12) and IL-4 play important roles in the development of Th1-like (type-1) and Th2-like (type-2) T-cell responses, respectively, and there is evidence that type-1/type-2 T helper imbalances are important in the pathogenesis of human immunodeficiency virus (HIV) disease. With this background, we examined the effects of these cytokines on HIV replication. Neither stimulated HIV replication in fresh peripheral blood mononuclear cells (PBMC). However, in prestimulated PBMC, IL-12, and to a greater extent, IL-4 as well as IL-2, induced production of HIV p24 antigen over 7 days of culture (no cytokine 3,900 x/divided by 1.31 [GM x/divided by SEM] pg/mL; IL-12, 34,300 x/divided by 1.39 pg/mL; IL-4, 283,000 x/divided by 1.14 pg/mL; and IL-2, 328,000 x/divided by 1.31 pg/mL). Neither IL-12- nor IL-4-induced HIV replication was attributable to induction of IL-1, IL-2, tumor necrosis factor (TNF)-alpha, or TNF-beta. Both IL-12- and IL-4-induced HIV replication was associated with selective loss of the CD4+ subset in

stimulated cultures. IL-4 stimulated HIV replication in monocyte/macrophages, while IL-12 had little or no effect in these cells. Finally, HIV replication stimulated by IL-12 or IL-4 was inhibited by dideoxynucleosides. Thus, IL-12 and IL-4 enhance HIV replication and HIV-induced cell death in prestimulated PBMC. Through killing of the CD4+ T cells stimulated by these cytokines, this may result in inappropriate type-1/type-2 responses in HIV-infected patients and contribute to their Th1 immunodeficiency.

CT Check Tags: Comparative Study; Human
Antibodies, Monoclonal: PD, pharmacology
Cells, Cultured
Cytopathogenic Effect, Viral: DE, drug effects
Didanosine: PD, pharmacology
HIV Core Protein p24: BI, biosynthesis
*HIV-1: DE, drug effects
HIV-1: PH, physiology
Interleukin-12: AI, antagonists & inhibitors
Interleukin-12: IM, immunology
*Interleukin-12: PD, pharmacology
Interleukin-4: AI, antagonists & inhibitors
Interleukin-4: IM, immunology
*Interleukin-4: PD, pharmacology
Interleukins: AI, antagonists & inhibitors
Interleukins: PD, pharmacology
*Leukocytes, Mononuclear: DE, drug effects
Leukocytes, Mononuclear: VI, virology
Lymphocyte Transformation
*Macrophages: DE, drug effects
Macrophages: VI, virology
*Monocytes: DE, drug effects
Monocytes: VI, virology
Muromonab-CD3: PD, pharmacology
Phytohemagglutinins: PD, pharmacology
*T-Lymphocytes, Helper-Inducer: PA, pathology
T-Lymphocytes, Helper-Inducer: VI, virology
*Virus Replication: DE, drug effects
Zalcitabine: PD, pharmacology
Zidovudine: PD, pharmacology

RN 30516-87-1 (Zidovudine); 69655-05-6 (Didanosine); 7481-89-2 (Zalcitabine)

CN 0 (Antibodies, Monoclonal); 0 (HIV Core Protein p24); 0 (Interleukin-12); 0 (Interleukin-4); 0 (Interleukins); 0 (Muromonab-CD3); 0 (Phytohemagglutinins)

L1 ANSWER 10 OF 11 MEDLINE

AN 94264312 MEDLINE

TI Interleukin-10 suppresses human immunodeficiency virus-1 replication in vitro in cells of the monocyte/macrophage lineage.

AU **Saville M W**; Taga K; Foli A; Broder S; Tosato G; Yarchoan R

CS Retroviral Diseases Section, National Cancer Institute, Bethesda, MD 20892.

SO BLOOD, (1994 Jun 15) 83 (12) 3591-9.
Journal code: A8G. ISSN: 0006-4971.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals

EM 9409

AB The cytokine interleukin-10 (IL-10) has been implicated in the pathogenesis of a number of disease states, including Epstein-Barr virus and human immunodeficiency virus (HIV-1) infections. In the acquired immunodeficiency syndrome (AIDS), it has been suggested that IL-10 may have a deleterious effect by suppressing cell-mediated immunity. However, there are few data on its direct

effects on HIV-1 replication. In the present study, we have found that recombinant human IL-10 (rhIL-10), present during days 0 through 2, potently inhibits HIV production in elutriated monocyte/macrophage (M/M) cultures with a 50% inhibitory concentration (IC50) of approximately 0.03 U/mL. This effect did not appear to be caused by toxicity to M/M because there was no change in cell viability, ability to phagocytose latex beads, or protein synthesis as measured by [3H]-leucine incorporation, at doses of rhIL-10 that inhibit viral replication. In addition, lipopolysaccharide-induced production of IL-1 beta, IL-6, or tumor necrosis factor-alpha was not affected at these doses, nor were human mononuclear cell proliferative responses to phytohemagglutinin, OKT3 antibody, or tetanus toxoid. HIV-1 replication was similarly decreased by rhIL-10 in the monocytoid line U937 without signs of cellular toxicity. However, these effects required much higher concentrations of rhIL-10, and viral production was only partially suppressed. rhIL-10 also slightly inhibited HIV-induced cytopathicity in ATH-8, a tetanus toxoid-specific, retrovirally immortalized T-cell line, but had no effect on HIV replication in the H9 and MOLT-4 T cell lines. Thus, rhIL-10 appears to inhibit HIV replication predominantly in cells of the M/M lineage. This effect may serve to reduce viral production in patients with AIDS. However, additional studies will be needed to more precisely define its physiologic role in this disease.

CT Check Tags: Human
Cells, Cultured
CD4-Positive T-Lymphocytes: MI, microbiology
*HIV-1: DE, drug effects
HIV-1: PH, physiology
*Interleukin-10: PD, pharmacology
Macrophages: DE, drug effects
Macrophages: MI, microbiology
Monocytes: DE, drug effects
Monocytes: MI, microbiology
Recombinant Proteins: PD, pharmacology
*Virus Replication: DE, drug effects

RN 130068-27-8 (Interleukin-10)

CN 0 (Recombinant Proteins)

L1 ANSWER 11 OF 11 MEDLINE

AN 94103671 MEDLINE

TI A randomized pilot study of alternating or simultaneous zidovudine and didanosine therapy in patients with symptomatic human immunodeficiency virus infection [published erratum appears in J Infect Dis 1994 Jul;170(1):260].

AU Yarchoan R; Lietzau J A; Nguyen B Y; Brawley O W; Pluda J M; **Saville M W**; Wyvill K M; Steinberg S M; Agbaria R; Mitsuya H; et al

CS National Institutes of Health, Bethesda, MD 20892.

SO JOURNAL OF INFECTIOUS DISEASES, (1994 Jan) 169 (1) 9-17. Journal code: IH3. ISSN: 0022-1899.

CY United States

DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 9404

AB A randomized pilot study comparing alternating and simultaneous regimens of zidovudine and didanosine (ddI) was conducted in 41 patients with AIDS or symptomatic human immunodeficiency virus (HIV) infection. Patients on each regimen received the same overall amounts of zidovudine and didanosine over time. CD4 cell counts in patients on the simultaneous regimen reached a maximum (mean +/- SE) of 108 +/- 16/mm3 above baseline (two-tailed P < or = .0001) and

were significantly higher than in patients on the alternating regimen at all time points during weeks 6-45. At 54 weeks, the CD4 cell counts in the patients on the simultaneous regimen were still 40 +/- 19/mm3 above baseline. Patients on the simultaneous regimen also had significantly greater weight gain. While toxicities were generally mild and comparable between the regimens, 1 patient on the simultaneous regimen died of pancreatitis and lactic acidosis. Thus, simultaneous therapy provided more sustained elevations in CD4 cells than alternating therapy over 1 year and may be worth exploring in larger controlled trials.

CT Check Tags: Comparative Study; Female; Human; Male
beta 2-Microglobulin: AN, analysis
Administration, Oral
Adolescence
Adult
AIDS-Related Opportunistic Infections
Body Weight: DE, drug effects
CD4-Positive T-Lymphocytes
Didanosine: AD, administration & dosage
Didanosine: AE, adverse effects
*Didanosine: TU, therapeutic use
Drug Administration Schedule
Drug Therapy, Combination
Follow-Up Studies
HIV Core Protein p24: BL, blood
*HIV Infections: DT, drug therapy
HIV Infections: IM, immunology
Leukocyte Count: DE, drug effects
Middle Age
Pancreatitis: CI, chemically induced
Pilot Projects
Zidovudine: AD, administration & dosage
Zidovudine: AE, adverse effects
*Zidovudine: TU, therapeutic use

RN 30516-87-1 (Zidovudine); 69655-05-6 (Didanosine)

CN 0 (beta 2-Microglobulin); 0 (HIV Core Protein p24)

L1 ANSWER 8 OF 11 MEDLINE
AN 95326733 MEDLINE
TI Treatment of HIV-associated Kaposi's sarcoma with paclitaxel.
AU **Saville M W**; Lietzau J; Pluda J M; Feuerstein I; Odom J; Wilson W H; Humphrey R W; Feigal E; Steinberg S M; Broder S; et al
CS National Cancer Institute, Bethesda, MD 20892, USA.
SO LANCET, (1995 Jul 1) 346 (8966) 26-8.
Journal code: L0S. ISSN: 0140-6736.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9510
AB We investigated whether paclitaxel was active in AIDS-associated Kaposi's sarcoma. We gave 135 mg/m2 intravenously over 3 hours every 21 days. Follow-up is available on the first 20 patients, most of whom had advanced Kaposi's sarcoma and severe immunocompromise. Neutropenia was the most frequent dose-limiting toxic effect; novel toxic effects included late fevers, rash, and eosinophilia. Creatinine increased in 2 patients and 1 patient had cardiomyopathy. There were 13 partial responses (65%, 95% CI 41-85%). All 5 patients with pulmonary involvement responded. Paclitaxel appears to be active against Kaposi's sarcoma as a single agent. Further studies, including a randomised trial, are warranted.
CT Check Tags: Human; Male; Support, Non-U.S. Gov't
Acquired Immunodeficiency Syndrome: CO, complications
Adult
Cimetidine: AD, administration & dosage
Dexamethasone: AD, administration & dosage
Diphenhydramine: AD, administration & dosage
Drug Therapy, Combination
*HIV Infections: CO, complications
*HIV-1
*Lung Neoplasms: DT, drug therapy
Middle Age
*Paclitaxel: AD, administration & dosage
Paclitaxel: AE, adverse effects
*Sarcoma, Kaposi's: DT, drug therapy
RN 33069-62-4 (Paclitaxel); 50-02-2 (Dexamethasone); 51481-61-9 (Cim

> d his

(FILE 'HOME' ENTERED AT 10:27:24 ON 22 SEP 1997)

FILE 'MEDLINE' ENTERED AT 10:27:33 ON 22 SEP 1997

		E	GILL P/AU
L1	2525	S	PACLITAXEL
L2	153	S	E3
L3	0	S	L2 AND L1
		E	GILL PARKASH S./AU
L4	0	S	L1 AND GILL
L5	0	S	L1 AND GILL/AU
		E	GILL/AU
L6	5	S	"KAPOSI'S SARCOMA"
L7	2572	S	KAPOSIS (W) SARCOMA OR KS
L8	0	S	L1 AND L7
L9	2049	S	TAXOL
L10	0	S	L7 AND L9
L11	1557	S	L1 AND L9
L12	57	S	METHOD AND L11
L13	0	S	L12 AND L7
L14	9005	S	NEUTROPENIA
L15	18	S	L7 AND L14
L16	0	S	L15 AND L9
L17	161	S	L14 AND L9
L18	5	S	METHOD AND L17
L19	47568	S	SARCOMA
L20	17	S	L11 AND L19
		E	ARBUCK/AU
L21	0	S	L7 AND E5
L22	10	S	E5 AND L11

d l12 54 49 47 31 6 all

L12 ANSWER 54 OF 57 MEDLINE
AN 87310566 MEDLINE
TI Phase I trial of **taxol** given as a 24-hour infusion every 21 days: responses observed in metastatic melanoma.
AU Wiernik P H; Schwartz E L; Einzig A; Strauman J J; Lipton R B; Dutcher J P
NC 2P30CA13330-15 (NCI)
SO JOURNAL OF CLINICAL ONCOLOGY, (1987 Aug) 5 (8) 1232-9. Journal code: JCO. ISSN: 0732-183X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8712
AB **Taxol**, a plant product, has significant activity against certain rodent and human xenograft tumors. It promotes microtubule assembly in vitro, in contrast to vinca alkaloids, which inhibit assembly. In this phase I study, **taxol** was administered as a 24-hour continuous intravenous (IV) infusion in 65 courses to 26 patients. A premedication regimen of dexamethasone, cimetidine, and diphenhydramine was used to prevent the acute hypersensitivity reactions observed in previous studies of **taxol**. Only one episode of mild stridor occurred in this study. Peripheral neuropathy was the dose-limiting toxicity and was observed in 40% of patients treated at a dose of 250 mg/m2. Significant neutropenia of brief duration was also common. Pharmacokinetic studies by a high-performance liquid chromatography (HPLC) **method** demonstrated that drug plasma concentrations increased during the 24-hour infusion and then declined rapidly. Peak plasma concentrations correlated with dose, and less than 5% of **taxol** was excreted in the urine. Most of the drug was bound to serum components. Partial responses of more than 3 months' duration were observed in four of 12 melanoma patients treated. The recommended phase II dose of **taxol** on this schedule is 250 mg/m2. Priority should be given to the study of **taxol** in melanoma.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Alkaloids: AD, administration & dosage
Alkaloids: AE, adverse effects
*Alkaloids: TU, therapeutic use
Antineoplastic Agents, Phytogenic: AD, administration & dosage
Antineoplastic Agents, Phytogenic: AE, adverse effects
*Antineoplastic Agents, Phytogenic: TU, therapeutic use
Cimetidine: AD, administration & dosage
Dexamethasone: AD, administration & dosage
Diphenhydramine: AD, administration & dosage
Drug Administration Schedule
Drug Evaluation
Drug Hypersensitivity: ET, etiology
Drug Hypersensitivity: PC, prevention & control
Infusions, Intravenous
Kinetics
Melanoma: DT, drug therapy
*Melanoma: SC, secondary
Neoplasms: DT, drug therapy
Nervous System Diseases: CI, chemically induced

Neutropenia: CI, chemically induced
RN **33069-62-4 (Paclitaxel)**; 50-02-2 (Dexamethasone); 51481-61-9 (Cimetidine); 58-73-1 (Diphenhydramine)
CN 0 (Alkaloids); 0 (Antineoplastic Agents, Phytogenic)

L12 ANSWER 49 OF 57 MEDLINE
AN 91242703 MEDLINE
TI Analysis of anticancer drugs in biological fluids: determination of **taxol** with application to clinical pharmacokinetics.
AU Rizzo J; Riley C; von Hoff D; Kuhn J; Phillips J; Brown T
CS Department of Pharmaceutical Chemistry, University of Kansas, Lawrence 66045-2504..
NC CA-09242 (NCI)
CM-57737 (NCI)
RR-01346 (NCRR)
SO JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS, (1990) 8 (2) 159-64.
Journal code: A2C. ISSN: 0731-7085.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9109
AB **Taxol**, a novel antimitotic, antitumor agent is currently undergoing Phase 1 clinical trials for the treatment of various tumors. An isocratic HPLC **method** has been developed for the determination of **taxol** in human plasma and urine. The **method** was then applied to the clinical pharmacokinetics of **taxol** following 6-h intravenous (i.v.) infusions at doses of 175 and 225 mg m-2. A mobile phase of methanol-acetate buffer (0.02 M, pH 4.5) (65:35, v/v) was used to elute a C8 column with detection at 227 nm. The sample preparation involved extraction with t-butyl methyl ether followed by further clean-up of the sample by solid-phase extraction. The **method** was linear from 0.10-10 microM injected, with a chromatographic run time of 6 min. The results obtained from the clinical study indicate that the plasma pharmacokinetics of **taxol** are best characterized by a two compartment open body model. Additionally, the present study resulted in the detection of a previously unreported peak which may be a metabolite of **taxol**.
CT Check Tags: Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
*Alkaloids: AN, analysis
Alkaloids: PK, pharmacokinetics
*Antineoplastic Agents, Phytogenic: AN, analysis
Antineoplastic Agents, Phytogenic: PK, pharmacokinetics
Chromatography, High Pressure Liquid
RN **33069-62-4 (Paclitaxel)**
CN 0 (Alkaloids); 0 (Antineoplastic Agents, Phytogenic)

L12 ANSWER 47 OF 57 MEDLINE
AN 92238024 MEDLINE
TI **Taxol**: an important new drug in the management of epithelial ovarian cancer.
AU Markman M
CS Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York..
SO YALE JOURNAL OF BIOLOGY AND MEDICINE, (1991 Nov-Dec) 64 (6) 583-90.
Ref: 38
Journal code: XR7. ISSN: 0044-0086.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English

FS Priority Journals
EM 9207
AB **Taxol**, an antineoplastic agent isolated from the Pacific yew, has been demonstrated in three phase 2 clinical trials to have major activity (30 percent overall response rate) in patients with ovarian cancer refractory to cisplatin. The major toxicities associated with the agent are neutropenia (dose-limiting), hypersensitivity reactions, peripheral sensory neuropathy, and cardiac arrhythmias. A recently reported phase 1 trial of the combination of cisplatin and **taxol** has defined acceptable doses for the two-drug combination to be tested against cisplatin and cyclophosphamide as frontline therapy of advanced ovarian cancer. **Taxol** has also been examined for intraperitoneal administration in patients with ovarian cancer, with a major pharmacokinetic advantage for peritoneal cavity exposure being demonstrated. Unfortunately, any future development of **taxol** as an antineoplastic agent in the management of ovarian cancer will be dependent on the finding of an alternative source of the drug, as the current **method** of obtaining **taxol** from the bark of the Pacific yew provides insufficient quantities for large-scale clinical use.
CT Check Tags: Female; Human
*Alkaloids: TU, therapeutic use
*Antineoplastic Agents, Phytogenic: TU, therapeutic use
Clinical Trials
Drug Evaluation
*Ovarian Neoplasms: DT, drug therapy
RN **33069-62-4 (Paclitaxel)**
CN 0 (Alkaloids); 0 (Antineoplastic Agents, Phytogenic)

L12 ANSWER 31 OF 57 MEDLINE
AN 95018321 MEDLINE
TI Computerized quantitation of synergism and antagonism of **taxol**, topotecan, and cisplatin against human teratocarcinoma cell growth: a rational approach to clinical protocol design [see comments].
CM Comment in: J Natl Cancer Inst 1994 Oct 19;86(2):1493-5
AU Chou T C; Motzer R J; Tong Y; Bosl G J
CS Molecular Pharmacology and Therapeutics Program, Memorial Sloan-Kettering Cancer Center, New York, NY 10021.
NC CA18856 (NCI)
CM57732 (NCI)
CA05826 (NCI)
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1994 Oct 19) 86 (20) 1517-24.
Journal code: J9J. ISSN: 0027-8874.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9501
AB BACKGROUND: Cisplatin-based induction chemotherapy may achieve a complete response (i.e., no sign of tumor following treatment) in 70%-80% of patients with germ cell tumors. However, only a minority of patients in whom the firstline regimens fail are cured with the salvage regimens. PURPOSE: The aim of these studies was to identify new agents or new regimens for the treatment of germ cell tumors by carrying out quantitative assessment in vitro of two promising new antitumor agents (**paclitaxel** [**Taxol**] and topotecan) and three more established agents (cisplatin, vincristine, and etoposide). These agents were used singly or in two- and three-drug combinations and were selected because they represent five distinct categories of antineoplastic mechanisms. METHODS: The combination index-isobologram **method**, which is based on the median-effect principle developed by Chou and

Talalay, was used for computerized data analysis. This **method** was selected because it takes into account both the potencies of each drug and combinations of these drugs and the shapes of their dose-effect curves. RESULTS: Synergism against the growth of teratocarcinoma cells resistant to cisplatin (833K/64CP10 cells) was greater than against the growth of parent 833K cells. The degrees of synergism were in the following order: cisplatin + topotecan > or = **paclitaxel** + cisplatin + topotecan > **paclitaxel** + topotecan > or = **paclitaxel** + etoposide > **paclitaxel** + cisplatin + etoposide > **paclitaxel** + cisplatin. All other combinations showed nearly additive effects or moderate antagonism. The degrees of antagonism were as follows: cisplatin + etoposide > or = **paclitaxel** + vincristine > **paclitaxel** + cisplatin + vincristine > cisplastin + vincristine. The combination of **paclitaxel** and cisplatin was synergistic against 833K/64CP10 cells and moderately antagonistic against 833K cells. Since the combination of **paclitaxel**, cisplatin, and topotecan and the two-component combinations of these drugs (cisplatin + topotecan and **paclitaxel** + topotecan) showed synergism stronger than that of other combinations, these three drugs were selected for illustrating detailed data analysis, using a computer software program developed in this institute. CONCLUSIONS AND IMPLICATIONS: Our findings suggest that, as a result of synergy, the doses of these agents needed to achieve an antitumor effect may be reduced by twofold to eightfold when these agents are given in combination. The present quantitative data analyses for synergism or antagonism provide a basis for a rational design of clinical protocols for combination chemotherapy in patients with advanced germ cell tumors.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Antineoplastic Agents: PD, pharmacology
Antineoplastic Agents, Combined: PD, pharmacology
Camptothecin: AA, analogs & derivatives
Camptothecin: PD, pharmacology
Cisplatin: PD, pharmacology
Computer Simulation
Dose-Response Relationship, Drug
Drug Administration Schedule
Drug Antagonism
Drug Synergism
Etoposide: PD, pharmacology
Paclitaxel: PD, pharmacology
*Teratocarcinoma: DT, drug therapy
Tumor Cells, Cultured
Vincristine: PD, pharmacology

RN 133242-28-1 (topotecan); 15663-27-1 (Cisplatin); **33069-62-4 (Paclitaxel)**; 33419-42-0 (Etoposide); 57-22-7 (Vincristine); 7689-03-4 (Camptothecin)

CN 0 (Antineoplastic Agents); 0 (Antineoplastic Agents, Combined)

L12 ANSWER 6 OF 57 MEDLINE

AN 97159606 MEDLINE

TI Preliminary results of a phase I/II clinical trial of **paclitaxel** and carboplatin in non-small cell lung cancer.

AU Natale R B

CS Department of Medical Oncology, University of Southern California/Kenneth Norris Jr Comprehensive Cancer Center, Los Angeles 90033, USA.

SO SEMINARS IN ONCOLOGY, (1996 Dec) 23 (6 Suppl 16) 51-4. Journal code: UN5. ISSN: 0093-7754.

CY United States

DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)

Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9705
EW 19970501
AB Forty-nine patients with non-small cell lung cancer were treated in a study designed to establish the maximum tolerated dose of outpatient **paclitaxel** (**Taxol**; Bristol-Myers Squibb Company, Princeton, NJ), given by 3-hour infusion, combined with a fixed dose of carboplatin (area under the concentration-time curve [AUC] = 6, Calvert **method**). The study population included 31 men and 18 women with previously untreated, unresectable stage III or IV non-small cell lung cancer. Patients had a median age of 62 years (age range, 46 to 81 years) and a median Southwest Oncology Group performance status of 1 (range, 0 to 2). With six to 10 patients treated at each dose level, **paclitaxel** was given at a starting dose of 150 mg/m2, and doses were escalated by 25-mg/m2 increments. The carboplatin dose was fixed at an AUC of 6. **Paclitaxel** 250 mg/m2 was established as the maximum tolerated dose of this combination, and severe (grade 3) sensory neuropathy was defined as the dose-limiting toxicity. Objective responses were documented in 26 of 42 patients with objectively measurable disease, for an overall response rate of 62%. Although these data are preliminary, this regimen appears to be efficacious and cost-effective, and warrants further study. **Paclitaxel** 225 mg/m2 combined with carboplatin (AUC = 6) every 3 weeks is recommended for follow-up phase II and III clinical trials.
CT Check Tags: Female; Human; Male
Aged
Aged, 80 and over
*Antineoplastic Agents, Combined: AD, administration & dosage
*Antineoplastic Agents, Phytogenic: AD, administration & dosage
Antineoplastic Agents, Phytogenic: TO, toxicity
Carboplatin: AD, administration & dosage
*Carcinoma, Non-Small-Cell Lung: DT, drug therapy
Drug Administration Schedule
Drug Tolerance
Infusions, Parenteral
*Lung Neoplasms: DT, drug therapy
Middle Age
***Paclitaxel: AD, administration & dosage**
Paclitaxel: TO, toxicity
Peripheral Nervous System Diseases: CI, chemically induced
RN **33069-62-4 (Paclitaxel)**; 41575-94-4 (Carboplatin)
CN 0 (Antineoplastic Agents, Combined); 0 (Antineoplastic Agents, Phytogenic)

=> d l18 1-5

L18 ANSWER 1 OF 5 MEDLINE
AN 97096378 MEDLINE
TI Preliminary results of a phase I/II clinical trial of paclitaxel and carboplatin in non-small cell lung cancer.
AU Natale R B
CS Department of Medical Oncology, University of Southern California/Kenneth Norris Jr Comprehensive Cancer Center, Los Angeles 90033, USA.
SO SEMINARS IN ONCOLOGY, (1996 Oct) 23 (5 Suppl 12) 2-6.
Journal code: UN5. ISSN: 0093-7754.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9711
EW 19971101

L18 ANSWER 2 OF 5 MEDLINE
AN 95166317 MEDLINE
TI [Favorable results of paclitaxel (**Taxol**) in patients with ovary carcinoma pretreated with platinum].
Gunstig effect van paclitaxel (**Taxol**) bij patienten met een met platina voorbehandeld ovariumcarcinoom.
AU Hoekman K; Huijskes R V; Burger C W; Verheijen R H; Pinedo H M; Vermorken J B
CS Afd. Geneeskundige Oncologie, Academisch Ziekenhuis Vrije Universiteit, Amsterdam..
SO NEDERLANDS TIJDSCHRIFT VOOR GENEESKUNDE, (1995 Feb 11) 139 (6) 272-8.
Journal code: NUK. ISSN: 0028-2162.
CY Netherlands
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA Dutch
EM 9505

L18 ANSWER 3 OF 5 MEDLINE
AN 93161294 MEDLINE
TI **Taxol** in ovarian cancer.
AU Runowicz C D; Wiernik P H; Einzig A I; Goldberg G L; Horwitz S B
CS Albert Einstein Cancer Center, Albert Einstein College of Medicine, Bronx, NY 10461..
SO CANCER, (1993 Feb 15) 71 (4 Suppl) 1591-6. Ref: 38
Journal code: CLZ. ISSN: 0008-543X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9305

L18 ANSWER 4 OF 5 MEDLINE
AN 92238024 MEDLINE
TI **Taxol**: an important new drug in the management of epithelial ovarian cancer.
AU Markman M
CS Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York..
SO YALE JOURNAL OF BIOLOGY AND MEDICINE, (1991 Nov-Dec) 64 (6) 583-90.
Ref: 38
Journal code: XR7. ISSN: 0044-0086.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9207

L18 ANSWER 5 OF 5 MEDLINE
AN 87310566 MEDLINE
TI Phase I trial of **taxol** given as a 24-hour infusion every 21 days: responses observed in metastatic melanoma.
AU Wiernik P H; Schwartz E L; Einzig A; Strauman J J; Lipton R B; Dutcher J P
NC 2P30CA13330-15 (NCI)
SO JOURNAL OF CLINICAL ONCOLOGY, (1987 Aug) 5 (8) 1232-9.
Journal code: JCO. ISSN: 0732-183X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8712

=> d l18 1-5 ab

L18 ANSWER 1 OF 5 MEDLINE
AB A phase I/II study was carried out to determine the maximum tolerated dose of paclitaxel (**Taxol**; Bristol-Myers Squibb Company, Princeton, NJ) in combination with a fixed dose of carboplatin (area under the concentration-time curve = 6 by Calvert **method**) given on an every-3-week schedule to patients with non-small cell lung cancer (NSCLC). Cohorts of patients were entered at increasing dose levels of paclitaxel: six at dose level I (paclitaxel 150 mg/m2), six at dose level 2 (paclitaxel 175 mg/m2), 11 at dose level 3 (paclitaxel 200 mg/ m2), 21 at dose level 4 (paclitaxel 225 mg/m2), and five at dose level 5 (paclitaxel 250 mg/m2). The patients comprised 31 men and 18 women with a median age of 62 years (age range, 46 to 81 years) and a median Southwest Oncology Group performance status of I (range, 0 to 2). Twenty-three patients had unresectable stage III NSCLC and 26 had stage IV NSCLC. Fortynine patients and 176 treatment courses are evaluable for toxicity. Grade 4 **neutropenia** or grade 3 arthralgias/ myalgias or sensory neuropathy were the most significant toxicities of therapy. In addition, two patients (dose levels 2 and 3) experienced acute chest pain, flushing, and hypotension, and had electrocardiogram changes during the paclitaxel infusion; one had mild creatine phosphokidnase MB elevation. Both recovered uneventfully, were not re-treated with paclitaxel, and account for two of only four hospitalizations for toxicity management in this trial. At this time, 42 patients with objectively measurable disease are evaluable for responses: two complete responses and 24 partial responses (62% objective response rate) have been observed. These data imply that the maximum tolerated dose of paclitaxel is 250 mg/m2 with dose-limiting toxicity consisting primarily of grade 3

osteo/arthralgias-myalgias or cumulative sensory neuropathy; paclitaxel at a dose of 225 mg/m2 given by 3-hour infusion combined with carboplatin at a calculated target area under the concentration-time curve of 6 is a well-tolerated outpatient treatment regimen and highly active in NSCLC; myelosuppression is mild and rarely dose limiting. Most notably, paclitaxel appears to decrease carboplatin's pharmacodynamic effects on thrombopoiesis.

L18 ANSWER 2 OF 5 MEDLINE

AB OBJECTIVE. To assess the anti-tumour and side effects of paclitaxel in patients with ovarian carcinoma, after prior treatment with al least one platinum-containing chemotherapy regimen. DESIGN. Phase II study. SETTING. Academic Hospital of the Free University, Amsterdam. **METHOD**. Fourteen of 55 patients with progressive ovarian carcinoma were treated with 135 mg/m2 and 41 with 175 mg/m2 paclitaxel. 9 patients by 24-hour and 46 by 3-hour intravenous infusion. RESULTS. In 9/55 (16%) patients an objective tumour response was obtained, which was complete in 1 patient. In 19/55 (35%) patients the disease stabilised. The serum CA 125 level was increased in 52 patients. In 33% of the patients the course of the serum CA 125 was an indication of the tumour response. The median duration of response was 8 months (range 4.1-13.1) and the median duration of survival was 11.3 months (range 0.3-28.2). Side effects of paclitaxel treatment were hair-loss, arthralgia and myalgia and **neutropenia** of short duration. In 76% of patients pre-existing neurosensory symptoms increased mildly or developed de novo. The neurotoxic effect appeared reversible in most instances after discontinuation of the paclitaxel treatment. CONCLUSION. In this rather unfavourable patient population, paclitaxel induced only 16% objective response. However, more than 50% of the patients did benefit from paclitaxel treatment, as a much larger group had long lasting disease stabilisation without symptoms or had reduction of symptoms. The treatment was well tolerated by most patients.

L18 ANSWER 3 OF 5 MEDLINE

AB **Taxol** is a structurally complex natural plant product with a novel mechanism of action. The supply of this drug is limited by its low abundance in the bark of the slow-growing yew tree from which it is extracted. The chemical complexity of **taxol** has hampered the development of a feasible process to synthesize large quantities. Analogues are being made from a precursor found in the needles of the yew tree. However, there is a need to develop a more efficient **method** to provide adequate supplies of this drug. This review article summarizes the preclinical and clinical studies of **taxol** in ovarian cancer. Phase I studies have identified the drug's toxicities. **Neutropenia** has been the dose-limiting toxicity in most trials, and premedications and longer infusion schedules have been used to reduce the incidence and severity of hypersensitivity reactions. The intraperitoneal administration of **taxol** in Phase I studies showed a pharmacologic advantage with acceptable toxicity. Its activity in ovarian cancer was noticed first in Phase I trials at the Albert Einstein College of Medicine and Johns Hopkins University. These observations led to Phase II testing, which documented response rates of 20-35% in patients with relapsed or refractory ovarian cancer. Phase III trials of **taxol** and cisplatin versus cyclophosphamide and cisplatin in untreated patients with ovarian cancer are in progress. Studies combining **taxol** with colony-stimulating factors and cisplatin are ongoing. **Taxol** is an important new drug in ovarian cancer. Its unique mechanism of action and toxicities make it an attractive agent to use in combination with currently active drugs. Future studies will determine the role of **taxol** in the management of this disease, but the widespread availability of this drug will depend on the development of a feasible synthetic process.

L18 ANSWER 4 OF 5 MEDLINE

AB **Taxol**, an antineoplastic agent isolated from the Pacific yew, has been demonstrated in three phase 2 clinical trials to have major activity (30 percent overall response rate) in patients with ovarian cancer refractory to cisplatin. The major toxicities associated with the agent are **neutropenia** (dose-limiting), hypersensitivity reactions, peripheral sensory neuropathy, and cardiac arrhythmias. A recently reported phase 1 trial of the combination of cisplatin and **taxol** has defined acceptable doses for the two-drug combination to be tested against cisplatin and cyclophosphamide as frontline therapy of advanced ovarian cancer. **Taxol** has also been examined for intraperitoneal administration in patients with ovarian cancer, with a major pharmacokinetic advantage for peritoneal cavity exposure being demonstrated. Unfortunately, any future development of **taxol** as an antineoplastic agent in the management of ovarian cancer will be dependent on the finding of an alternative source of the drug, as the current **method** of obtaining **taxol** from the bark of the Pacific yew provides insufficient quantities for large-scale clinical use.

L18 ANSWER 5 OF 5 MEDLINE

AB **Taxol**, a plant product, has significant activity against certain rodent and human xenograft tumors. It promotes microtubule assembly in vitro, in contrast to vinca alkaloids, which inhibit assembly. In this phase I study, **taxol** was administered as a 24-hour continuous intravenous (IV) infusion in 65 courses to 26 patients. A premedication regimen of dexamethasone, cimetidine, and diphenhydramine was used to prevent the acute hypersensitivity reactions observed in previous studies of **taxol**. Only one episode of mild stridor occurred in this study. Peripheral neuropathy was the dose-limiting toxicity and was observed in 40% of patients treated at a dose of 250 mg/m2. Significant **neutropenia** of brief duration was also common. Pharmacokinetic studies by a high-performance liquid chromatography (HPLC) **method** demonstrated that drug plasma concentrations increased during the 24-hour infusion and then declined rapidly. Peak plasma concentrations correlated with dose, and less than 5% of **taxol** was excreted in the urine. Most of the drug was bound to serum components. Partial responses of more than 3 months' duration were observed in four of 12 melanoma patients treated. The recommended phase II dose of **taxol** on this schedule is 250 mg/m2. Priority should be given to the study of **taxol** in

0 ANSWER 5 OF 17 MEDLINE
AN 96228966 MEDLINE
TI **Paclitaxel**: current developmental approaches of the National Cancer Institute.
AU Arbuck S G
CS Investigational Drug Branch, National Cancer Institute, Bethesda, MD, USA.
SO SEMINARS IN ONCOLOGY, (1995 Dec) 22 (6 Suppl 15) 55-63.
Journal code: UN5. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9609
AB National Cancer Institute studies are addressing important issues in the development of **paclitaxel** (**Taxol**; Bristol-Myers Squibb Company, Princeton, NJ), including optimal dose and schedule, the development of combination chemotherapy and multimodality regimens, and the evaluation of **paclitaxel** -containing therapy as front-line and adjuvant treatment. Phase III trials are ongoing in ovary, breast, lung, and head and neck cancers. Broad phase II testing of **paclitaxel** is nearing completion. Recent identification of **paclitaxel** activity in esophageal, bladder, germ cell, and endometrial cancers and in Kaposi's **sarcoma** associated with the human immunodeficiency virus has provided additional areas for investigation. Promising results from initial trials provide reasons to expect further advances as investigators around the world continue to evaluate this important new drug.
CT Check Tags: Female; Human
Antineoplastic Agents, Combined: TU, therapeutic use
Antineoplastic Agents, Phytogenic: AD, administration & dosage
*Antineoplastic Agents, Phytogenic: TU, therapeutic use
AIDS-Related Opportunistic Infections: DT, drug therapy
Bladder Neoplasms: DT, drug therapy
Breast Neoplasms: DT, drug therapy
Chemotherapy, Adjuvant
Clinical Trials, Phase II
Clinical Trials, Phase III
Combined Modality Therapy
Drug Administration Schedule
Endometrial Neoplasms: DT, drug therapy
Esophageal Neoplasms: DT, drug therapy
Germinoma: DT, drug therapy
Head and Neck Neoplasms: DT, drug therapy
Lung Neoplasms: DT, drug therapy
*National Institutes of Health (U.S.)
Ovarian Neoplasms: DT, drug therapy
Paclitaxel: AD, administration & dosage
***Paclitaxel: TU, therapeutic use**
Sarcoma, Kaposi's: DT, drug therapy
United States
RN **33069-62-4 (Paclitaxel)**
CN 0 (Antineoplastic Agents, Combined); 0 (Antineoplastic Agents, Phyt

L22 ANSWER 2 OF 10 MEDLINE
AN 95169622 MEDLINE
TI **Taxol** (**paclitaxel**): future directions.
AU **Arbuck S G**
CS Investigational Drug Branch, National Cancer Institute, Bethesda, Maryland..
SO ANNALS OF ONCOLOGY, (1994) 5 Suppl 6 S59-62. Ref: 30
Journal code: AYF. ISSN: 0923-7534.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9506
AB **Paclitaxel** is the first of a new class of anticancer agents with a novel mechanism of action. Demonstration of the broad activity of this drug and its unusual effects has refocused attention on tubulin as a target for anticancer drug development. Studies are under way to identify the optimal **paclitaxel** dose and schedule of administration and the effective combination regimens, and to exploit the drug's radiosensitizing properties. Efforts to define pharmacodynamic relationships and clinical mechanisms of resistance and to assess other potential mechanisms for the drug's anticancer activity are also under way. In addition, other compounds that target the microtubule, some more soluble and some more potent, are in various stages of development. Phase III trials in patients with ovarian, breast, and lung cancer are continuing, and adjuvant breast cancer trials will begin soon. Such trials will establish whether **paclitaxel** increases the cure rate and/or survival in cancer patients.
CT Check Tags: Female; Human
Antineoplastic Agents, Combined: TU, therapeutic use
*Breast Neoplasms: DT, drug therapy
Breast Neoplasms: RT, radiotherapy
Clinical Trials, Phase III
Combined Modality Therapy
Dose-Response Relationship, Drug
Drug Administration Schedule
Drug Resistance
Forecasting
*Lung Neoplasms: DT, drug therapy
Lung Neoplasms: RT, radiotherapy
*Ovarian Neoplasms: DT, drug therapy
Ovarian Neoplasms: RT, radiotherapy
Paclitaxel: PD, pharmacology
***Paclitaxel: TU, therapeutic use**
RN **33069-62-4 (Paclitaxel)**
CN 0 (Antineoplastic Agents, Combined)

L22 ANSWER 3 OF 10 MEDLINE
AN 95137486 MEDLINE
TI Options for primary chemotherapy of epithelial ovarian cancer: taxanes.
AU Trimble E L; **Arbuck S G**; McGuire W P
CS Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, Maryland 20892..
SO GYNECOLOGIC ONCOLOGY, (1994 Dec) 55 (3 Pt 2) S114-21. Ref: 44
Journal code: FXC. ISSN: 0090-8258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals

EM 9505
AB The taxanes, a new class of anticancer agents, act by promoting the assembly of microtubules and stabilizing formed tubules. Two taxanes, **paclitaxel** and docetaxel, have clinical activity in epithelial ovarian carcinomas, including tumors with platinum resistance. Toxicities associated with the taxanes include hypersensitivity, leukopenia, neurotoxicity, and alopecia. Premedication with dexamethasone, diphenhydramine, and cimetidine decreases the incidence of severe anaphylactic reactions to less than 3%. In Phase II studies, response rates to **paclitaxel** in patients with previously treated ovarian cancer ranged from 20 to 48%. To date, only two Phase III study using **paclitaxel** in the treatment of ovarian cancer have mature data. In one trial in patients with suboptimally debulked stage III and IV ovarian cancer, conducted by the Gynecologic Oncology Group, patients receiving **paclitaxel**/cisplatin had a significantly greater clinical response rate and surgical response rate and a significantly smaller risk of progression than those of patients receiving cisplatin/cyclophosphamide. In a Phase III study of **paclitaxel** in previously treated patients at two different schedules (3- and 24-hr infusions), conducted by the Canadian-European **Taxol** Cooperative Group, patients on the 24-hr infusion experienced significantly more grade 4 neutropenia than those receiving the 3-hr infusion. The optimal dose, schedule, and combination for **paclitaxel** in the treatment of patients with ovarian cancer have not yet been defined. In Phase II studies of docetaxel in patients with previously treated ovarian cancer, response rates of 33-35% were noted. Peripheral edema was noted to be a clinically significant toxicity.
CT Check Tags: Female; Human
Antineoplastic Agents, Combined: TU, therapeutic use
*Antineoplastic Agents, Phytogenic: TU, therapeutic use
*Bicyclo Compounds: TU, therapeutic use
Cisplatin: AD, administration & dosage
*Ovarian Neoplasms: DT, drug therapy
Paclitaxel: AA, analogs & derivatives
Paclitaxel: AD, administration & dosage
Paclitaxel: AE, adverse effects
Paclitaxel: TU, therapeutic use
Remission Induction
RN 114977-28-5 (docetaxel); 15663-27-1 (Cisplatin); 1605-68-1 (taxane); **33069-62-4 (Paclitaxel)**
CN 0 (Antineoplastic Agents, Combined); 0 (Antineoplastic Agents, Phytogenic); 0 (Bicyclo Compounds)

L22 ANSWER 4 OF 10 MEDLINE
AN 94289126 MEDLINE
TI **Taxol**: a history of pharmaceutical development and current pharmaceutical concerns.
AU Adams J D; Flora K P; Goldspiel B R; Wilson J W; **Arbuck S G**; Finley R
CS Drug Management and Authorization Section, National Cancer Institute, Bethesda, MD 20892.
SO MONOGRAPHS / NATIONAL CANCER INSTITUTE, (1993) (15) 141-7. Ref: 40
Journal code: ATR. ISSN: 1052-6773.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9410
AB **Taxol**, a unique diterpene anticancer compound derived from the bark of the Taxus brevifolia (Pacific yew) tree, induces cytotoxicity by a novel mechanism of action. An antimicrotubule

agent, **Taxol** promotes the formation and stabilization of the tubulin polymer unlike other anticancer agents that induce microtubule disassembly. Because of its poor aqueous solubility, **Taxol** is formulated as a solution in 50% Cremophor EL and 50% dehydrated alcohol, USP. The Cremophor EL and dehydrated alcohol vehicle used in the formulation of **Taxol** creates some interesting challenges for its preparation and administration. The pharmaceutical concerns associated with the preparation and administration of **Taxol** are discussed.

CT Check Tags: Animal; Human
Chemistry, Pharmaceutical
Drug Incompatibility
Drug Stability
Paclitaxel: AD, administration & dosage
***Paclitaxel: CH, chemistry**
Paclitaxel: TO, toxicity
Solubility

RN **33069-62-4 (Paclitaxel)**

L22 ANSWER 5 OF 10 MEDLINE
AN 94289124 MEDLINE
TI A reassessment of cardiac toxicity associated with **Taxol**.
AU **Arbuck S G**; Strauss H; Rowinsky E; Christian M; Suffness M; Adams J; Oakes M; McGuire W; Reed E; Gibbs H; et al
CS Investigational Drug Branch, National Cancer Institute, Bethesda, MD 20892.
SO MONOGRAPHS / NATIONAL CANCER INSTITUTE, (1993) (15) 117-30. Ref: 38
Journal code: ATR. ISSN: 1052-6773.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9410
AB Cardiac toxicity was first noted in patients receiving **Taxol** during continuous cardiac monitoring, which was performed because of the high incidence of serious hypersensitivity reactions noted early in phase I trials. After cardiac events were documented, patients with cardiac disease and those on medications known to alter cardiac conduction were excluded from most trials. The cardiac events reported with **Taxol** from the initiation of NCI-sponsored clinical trials through August 1992 are summarized. Adverse cardiac events were reviewed in four clinical databases: 1) the Cancer Therapy Evaluation Program's Adverse Drug Reaction database following treatment of more than 3400 patients; 2) all cardiac toxicities in patients on GOG-111 who were randomized to cisplatin plus either **Taxol** or cyclophosphamide; 3) cardiac toxicity in 198 patients who received 618 courses of **Taxol** with or without cisplatin during continuous cardiac monitoring; and 4) cardiac toxicities reported for the first 696 patients on NCI TRC-9103 for ovarian cancer. Published reports of studies of taxine's cardiac effects, and of cardiac toxicity associated with yew poisoning, Cremophor EL, and H1 and H2 antagonists, are also reviewed. In patients without significant cardiac risk factors, asymptomatic sinus bradycardia is frequent (approximately 30%). Heart block and conduction abnormalities occur infrequently and are often asymptomatic. The casual relationship of **Taxol** to atrial and ventricular arrhythmias and cardiac ischemia is less clear because many patients had other conditions known to be associated with cardiac events. Nevertheless, the incidence of serious cardiac events was low. Routine cardiac monitoring is not required for patients without risk factors. There are, however, insufficient data to make treatment recommendations for patients with cardiac disease and those taking medications that alter cardiac

conduction. To maximize patient safety and the clinical database, physicians who administer **Taxol** should continue to be alert to potential cardiac toxicities associated with **Taxol**
.

CT Check Tags: Animal; Female; Human
Arrhythmia: CI, chemically induced
*Heart Diseases: CI, chemically induced
Myocardial Infarction: CI, chemically induced
Ovarian Neoplasms: DT, drug therapy
Paclitaxel: AD, administration & dosage
***Paclitaxel: AE, adverse effects**
Polyethylene Glycols: AD, administration & dosage
RN **33069-62-4 (Paclitaxel)**; 39279-69-1 (cremophor)
CN 0 (Polyethylene Glycols)

L22 ANSWER 6 OF 10 MEDLINE
AN 94289123 MEDLINE
TI Clinical development of **Taxol**.
AU **Arbuck S G**; Christian M C; Fisherman J S; Cazenave L A; Sarosy G; Suffness M; Adams J; Canetta R; Cole K E; Friedman M A
CS M. A. Friedman, Cancer Therapy Evaluation Program, Division of Cancer Treatment, National Cancer Institute, Bethesda, MD 20892.
SO MONOGRAPHS / NATIONAL CANCER INSTITUTE, (1993) (15) 11-24. Ref: 90
Journal code: ATR. ISSN: 1052-6773.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9410
AB **Taxol** is the first of a novel class of anticancer drugs, the taxanes. **Taxol**'s unique effects include its ability to polymerize tubulin into stable microtubules in the absence of cofactors and to induce the formation of stable microtubule bundles. During its development, formidable challenges were overcome: a suitable formulation was developed, an adequate supply was ensured, severe hypersensitivity reactions were diminished in incidence and severity, and clinical efficacy was demonstrated. Phase II evaluation is still underway; to date, clinical efficacy has been demonstrated in ovarian, breast, non-small-cell lung, and head and neck cancer. Response rates were low in early studies in melanoma, prostate, colon, cervix, and renal cancer, but for these tumors, additional evaluation is ongoing with a higher **Taxol** dose or different schedule. In December 1992, Food and Drug Administration approval was granted for use of **Taxol** as second-line therapy in ovarian cancer patients. Nevertheless, important questions regarding optimal use of this important new drug remain. These include determination of optimal dose and schedule and development of suitable combination chemotherapy regimens. The clinical development of **Taxol** and current status of phase I, II, and III clinical trials are reviewed.
CT Check Tags: Animal; Human
Clinical Trials
*Neoplasms: DT, drug therapy
Paclitaxel: AE, adverse effects
Paclitaxel: PD, pharmacology
***Paclitaxel: TU, therapeutic use**
RN **33069-62-4 (Paclitaxel)**

L22 ANSWER 7 OF 10 MEDLINE
AN 94201161 MEDLINE
TI **Paclitaxel** (**Taxol**) in breast cancer.
AU **Arbuck S G**; Dorr A; Friedman M A
CS Cancer Therapy Evaluation Program, National Cancer Institute,

Bethesda, Maryland..
SO HEMATOLOGY/ONCOLOGY CLINICS OF NORTH AMERICA, (1994 Feb) 8 (1) 121-40. Ref: 67
Journal code: HEO. ISSN: 0889-8588.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9407
AB **Paclitaxel** (**Taxol**) is a diterpine plant compound that was isolated initially from the bark of the western yew tree, Taxus brevifolia, but can now be produced by semisynthesis from a renewable source. **Paclitaxel** is the first new agent in the past decade to have confirmed single agent activity in breast cancer in excess of 50%. A 28% response rate has been reported in doxorubicin-refractory patients. Ongoing studies include attempts to combine **paclitaxel** with other drugs used for breast cancer treatment and with radiation.
CT Check Tags: Female; Human
*Breast Neoplasms: DT, drug therapy
Breast Neoplasms: PA, pathology
Clinical Trials
Drug Resistance
Neoplasm Metastasis
***Paclitaxel: TU, therapeutic use**
Radiation-Sensitizing Agents: TU, therapeutic use
RN **33069-62-4 (Paclitaxel)**
CN 0 (Radiation-Sensitizing Agents)

L22 ANSWER 8 OF 10 MEDLINE
AN 93342552 MEDLINE
TI Current dosage and schedule issues in the development of **paclitaxel** (**Taxol**).
AU **Arbuck S G**; Canetta R; Onetto N; Christian M C
CS Developmental Chemotherapy Section, National Cancer Institute, Bethesda, MD 20892..
SO SEMINARS IN ONCOLOGY, (1993 Aug) 20 (4 Suppl 3) 31-9. Ref: 52
Journal code: UN5. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 9311
AB Basic questions regarding optimal dose and schedule of anticancer drug administration frequently persist long after regulatory approval and commercial availability of a drug. For **paclitaxel** (**TAXOL**), these questions were considered early in drug development. This paper reviews the available preclinical studies that assessed different drug concentrations and durations of drug exposure. The current status of clinical trials designed to help resolve these issues is also reviewed.
CT Check Tags: Animal; Human
Bone Marrow Diseases: CI, chemically induced
Clinical Trials
Dogs
Dose-Response Relationship, Drug
Drug Evaluation
Drug Hypersensitivity: ET, etiology
Drug Screening
Mice

Microtubules: DE, drug effects
*Neoplasms: DT, drug therapy
***Paclitaxel*: AD, administration & dosage**
Paclitaxel: AE, adverse effects
Peripheral Nervous System Diseases: CI, chemically induced
Rats
Time Factors
RN **33069-62-4 (Paclitaxel)**

L22 ANSWER 9 OF 10 MEDLINE
AN 93342548 MEDLINE
TI Clinical toxicities encountered with **paclitaxel** (**Taxol**).
AU Rowinsky E K; Eisenhauer E A; Chaudhry V; **Arbuck S G**; Donehower R C
CS Johns Hopkins Oncology Center, Division of Pharmacology and Experimental Therapeutics, Baltimore, MD 21287-8934.
SO SEMINARS IN ONCOLOGY, (1993 Aug) 20 (4 Suppl 3) 1-15. Ref: 58
Journal code: UN5. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals; Cancer Journals
EM 9311
AB Although **paclitaxel** (**TAXOL**) appears to be one of the most promising antineoplastic agents of the last decade, with demonstrated activity in advanced and refractory ovarian, breast, lung, and head and neck cancers, most clinical oncologists have had little experience with the agent. This is largely the result of the initially limited supply of **paclitaxel** and other obstacles encountered during early clinical development that restricted the drug's availability to a few investigational centers. Although a high incidence of major hypersensitivity reactions due to the Cremophor EL vehicle used in formulation disrupted and almost terminated the clinical development of **paclitaxel**, hypersensitivity reactions are no longer a serious problem consequent to the advent of effective premedication regimens and longer administration schemes. Instead, neutropenia is the principal toxicity of **paclitaxel**. At clinically relevant doses, absolute neutrophil count nadirs are severely depressed in most patients. The duration of severe neutropenia, however, is usually brief; treatment delays for unresolved hematologic toxicity are rare, and absolute neutrophil count nadirs are constant with repetitive dosing, suggesting that neutropenia is not cumulative. Asymptomatic sinus bradycardia has occurred in up to 29% of patients in phase II trials, and other cardiac disturbances, including atrioventricular conduction and bundle branch blocks, ventricular tachycardia, and possible ischemic manifestations, have been reported in approximately 3% of patients. Cardiac disturbances have primarily been noted in studies that used cardiac monitoring to more effectively detect and manage major hypersensitivity reactions. Although sinus bradycardia and conduction blocks appear to represent true toxicities, ventricular tachycardia and ischemic manifestations, which have largely been observed in patients with preexisting cardiac disease, may not be due to **paclitaxel**. In view of the lack of clinical significance of the cardiac effects and their infrequent occurrence, cardiac monitoring during **paclitaxel** is not recommended for patients without cardiac risk factors. However, until precise risk factors can be defined, patients with a significant antecedent cardiac history are generally not considered to be good candidates for **paclitaxel** therapy. Neurotoxicity, characterized principally by peripheral neurosensory manifestations, has generally been of mild to moderate

severity, even in heavily pretreated patients at **paclitaxel** doses < or = 200 mg/m2. However, some patients have developed a severe sensory-motor polyneuropathy at higher doses of **paclitaxel** (given as a single agent or in combination with cisplatin). Patients with an antecedent peripheral neuropathy or coexisting medical illnesses associated with peripheral neuropathy (such as diabetes mellitus and substantial prior alcohol use) appear to be especially prone to developing peripheral neuropathy.(ABSTRACT TRUNCATED AT 400 WORDS)

CT Check Tags: Human
Alopecia: CI, chemically induced
Arrhythmia: CI, chemically induced
Brain Diseases: CI, chemically induced
Clinical Trials
Drug Administration Schedule
Drug Hypersensitivity: ET, etiology
Gastrointestinal Diseases: CI, chemically induced
IgE: BI, biosynthesis
Models, Biological
Muscular Diseases: CI, chemically induced
*Neoplasms: DT, drug therapy
Neutropenia: CI, chemically induced
Paclitaxel: AD, administration & dosage
***Paclitaxel: AE, adverse effects**
Peripheral Nervous System Diseases: CI, chemically induced
Risk Factors

RN **33069-62-4 (Paclitaxel)**; 37341-29-0 (IgE)

L22 ANSWER 10 OF 10 MEDLINE
AN 93097141 MEDLINE
TI **Taxol**: the first of the taxanes, an important new class of antitumor agents.
AU Rowinsky E K; Onetto N; Canetta R M; **Arbuck S G**
CS Division of Pharmacology and Experimental Therapeutics, Johns Hopkins Oncology Center, Baltimore, MD 21205..
SO SEMINARS IN ONCOLOGY, (1992 Dec) 19 (6) 646-62. Ref: 56
Journal code: UN5. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 9303
AB The taxanes represent the first class of antimicrotubule agents with a new mechanism of cytotoxic action since the introduction of the vinca alkaloids several decades ago. These compounds may prove to be the "anticancer drugs of the 1990s," just as the anthracyclines and the platinum compounds were the "anticancer drugs" of the 1970s and 1980s. Like the platinums, **taxol**, the prototypic taxane, has shown significant antineoplastic activity in patients with advanced ovarian cancer, with response rates ranging from 20% to 50%. Moreover, **taxol** has been shown to be useful in patients with platinum-resistant ovarian cancer. Although phase II screening is not yet complete, the results of phase II studies of **taxol** in advanced cancers of the ovary, breast (response rates, 56% to 62%), and lung (response rates, 21% to 24%) have rekindled interest in the microtubule as a prime strategic target for cancer therapy. After briefly reviewing the mechanisms of antineoplastic action and resistance and the results of preliminary clinical and pharmacological studies, this review will discuss several critical issues that will be addressed in future clinical trials, developmental directions, and drug supply. Although this review will focus primarily on **taxol**, the results of preliminary investigations with the semisynthetic taxane analog

taxotere will also be discussed.

CT Check Tags: Animal; Female; Human
Antineoplastic Agents, Phytogenic: TU, therapeutic use
Breast Neoplasms: DT, drug therapy
Clinical Trials
Drug Evaluation
Drug Screening
*Drugs, Investigational
Drugs, Investigational: CH, chemistry
Drugs, Investigational: PD, pharmacology
Drugs, Investigational: TU, therapeutic use
Forecasting
Lung Neoplasms: DT, drug therapy
*Neoplasms: DT, drug therapy
Ovarian Neoplasms: DT, drug therapy
***Paclitaxel**
Paclitaxel: AA, analogs & derivatives
Paclitaxel: CH, chemistry
Paclitaxel: PD, pharmacology
Paclitaxel: PH, physiology
Paclitaxel: TU, therapeutic use

RN 114977-28-5 (docetaxel); **33069-62-4 (Paclitaxel)**

CN 0 (Antineoplastic Agents, Phytogenic); 0 (Drugs, Investigational)

d l22 1-10 all

L22 ANSWER 1 OF 10 MEDLINE
AN 96228966 MEDLINE
TI **Paclitaxel**: current developmental approaches of the National Cancer Institute.
AU **Arbuck S G**
CS Investigational Drug Branch, National Cancer Institute, Bethesda, MD, USA.
SO SEMINARS IN ONCOLOGY, (1995 Dec) 22 (6 Suppl 15) 55-63. Journal code: UN5. ISSN: 0093-7754.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9609
AB National Cancer Institute studies are addressing important issues in the development of **paclitaxel** (**Taxol**; Bristol-Myers Squibb Company, Princeton, NJ), including optimal dose and schedule, the development of combination chemotherapy and multimodality regimens, and the evaluation of **paclitaxel** -containing therapy as front-line and adjuvant treatment. Phase III trials are ongoing in ovary, breast, lung, and head and neck cancers. Broad phase II testing of **paclitaxel** is nearing completion. Recent identification of **paclitaxel** activity in esophageal, bladder, germ cell, and endometrial cancers and in Kaposi's sarcoma associated with the human immunodeficiency virus has provided additional areas for investigation. Promising results from initial trials provide reasons to expect further advances as investigators around the world continue to evaluate this important new drug.
CT Check Tags: Female; Human
Antineoplastic Agents, Combined: TU, therapeutic use
Antineoplastic Agents, Phytogenic: AD, administration & dosage
*Antineoplastic Agents, Phytogenic: TU, therapeutic use
AIDS-Related Opportunistic Infections: DT, drug therapy
Bladder Neoplasms: DT, drug therapy
Breast Neoplasms: DT, drug therapy
Chemotherapy, Adjuvant
Clinical Trials, Phase II
Clinical Trials, Phase III
Combined Modality Therapy
Drug Administration Schedule
Endometrial Neoplasms: DT, drug therapy
Esophageal Neoplasms: DT, drug therapy
Germinoma: DT, drug therapy
Head and Neck Neoplasms: DT, drug therapy
Lung Neoplasms: DT, drug therapy
*National Institutes of Health (U.S.)
Ovarian Neoplasms: DT, drug therapy
Paclitaxel: AD, administration & dosage
***Paclitaxel: TU, therapeutic use**
Sarcoma, Kaposi's: DT, drug therapy
United States
RN **33069-62-4 (Paclitaxel)**
CN 0 (Antineoplastic Agents, Combined); 0 (Antineoplastic Agents, Phytogenic)